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Toni-Junell Herbert
REED SMITH
3110 Fairview Park Drive
Suite1400
Falls Church, VA 22042

EXAMINER	
HINES, JANA A	
ART UNIT	**PAPER NUMBER**
1645	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/026,914	LINHART ET AL.	
	Examiner	Art Unit	
	Ja-Na Hines	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 March 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *7,9,22-25 and 36-47* is/are pending in the application.

4a) Of the above claim(s) *7,9,22-25,36-41 and 44* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *42, 43 and 45-47* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Amendment Entry

1. The amendment filed March 27, 2007 has been entered. Claims 1-6, 8 10-21, 26-35 and 48-51 have been cancelled. Claims 7, 9, 22-25, 36-41 and 44 have been withdrawn. Claims 42, 43 and 45 have been amended. Claims 42-43 and 45-47 are under consideration in this office action.

Response to Arguments

2. Applicant's arguments filed March 27, 2007 have been fully considered but they are not persuasive.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 42-43 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Claims 42-43 are drawn to a method of preparing fusion polypeptides consisting of timothy grass pollen allergens for use as immunotherapeutic agents comprising:

(a) providing a polynucleotide sequence encoding the fusion polypeptide; (b) introducing said polynucleotide sequence into a host cell; (c) culturing the host cell obtained in b) under conditions such that the fusion polypeptide is expressed; (d) recovering the expressed fusion polypeptide from the cultured host cell; and (e) testing the fusion polypeptide as candidate immunotherapeutic agents by administering said polypeptide to a test animal and selecting as immunotherapeutic agents those fusion polypeptides that induce IgE-blocking antibodies and induce stronger immune responses compared with the individual components or fragments thereof.

No information, beyond the characterization of a polypeptide having the ability to encode a fusion polypeptide have been provided, which would indicate that applicants did not have possession of the claimed genus of any polynucleotide sequences. The specification does not contain the disclosure of the structure of all polynucleotide sequences that encode a fusion polypeptide, which is within the scope of the claimed genus. The genus of encoding polynucleotide sequences claimed is a large variable genus including mutants and variants, which can have wide variety of structures. The specification discloses the structure of only 2 representative species i.e., drawn to Phlp1/Phlp5 and Phl p2/ Phl p6. The claims refer to individual components, however there is no description of what the individual components are. There is no disclosure of what the exact make-up of the fusion polypeptide is. Such is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that

applicant had possession of the claimed invention at the time the instant application was filed.

The specification and claims lack sufficient written description of the polynucleotide encoding the fusion polypeptide. The instant specification does not provide for the structure of the polynucleotide. The specification does not provide a teaching of the entire structure, showing that nucleic acids were isolated at the time the invention was made. The specification does not contain a structural characterization of the complete sequence. There is no adequate description of the nucleic acids which must encode the polypeptide. Since the claim language embraces lots of variants and there is no description of the nucleic acids which encodes such, the description is insufficient since there is no structure described. The polynucleotide is described by its function, i.e., the ability to encode the fusion polypeptide; this description is not sufficient to define the polynucleotide itself. The description of the ability of the claimed nucleic acid to encode the hybrid polypeptide may describe the polynucleotides function; however it does not describe the polynucleotide itself. The encoding distinction is a purely functional distinction. Thus, a description of the polynucleotide sequence by what is does, such as encoding a fusion polypeptide is insufficient. Furthermore, the claims recite selecting as immunotherapeutic agents those fusion polypeptides that induce IgE-blocking antibodies and induce stronger immune responses compared with the individual components or fragments thereof. However this selection distinction is a purely functional distinction. The description of the selection of immunotherapeutics is based on inducing IgE-blocking antibodies and stronger immune responses function;

however the selection criteria does not describe the polynucleotide itself. Thus the functional description fails to provide a physical structure or provide a critical feature within the polynucleotide sequence that allows for inducing IgE-blocking antibodies and creating stronger immune responses.

Moreover, the specification fails to describe any other representative species by any identifying characteristics or properties other than the functionality of the polynucleotide encoding a fusion polypeptide. The MPEP further states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP 2163. The MPEP does state that for generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. MPEP 2163. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP 2163. Although the MPEP does not define what constitute a sufficient number of representative, the Courts have indicated what do not constitute a representative number species to adequately describe a broad generic. In *Gostelli*, the Court determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. *In re Gostelli*, 872 F.2d at 1012, 10 USPQ2d at 1618. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 115).

Given this lack of description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention. The specification fails to teach what the critical nucleic acids can or cannot be modified and still achieve a functional fusion polypeptide. The specification fails to teach which residues of the sequence can be varied and still achieve a functional polypeptide. The specification has not conceived of any other functionally equivalent polynucleotide sequences encoding polypeptides, thus there is no teaching of where substitutions should be made. Thus the specification fails to enable the skilled artisan to envision the detailed chemical structure of the claimed structure of the claimed polynucleotide. The skilled artisan would be forced into undue experimentation to make and use the instantly claimed invention. The specification fails to provide guidance on how any nucleic acid can be substituted or inserted for the production of a polypeptide nor does the specification provide guidance on how any location can be used to produce an immunogenic polypeptide. There is no recitation of specific locations for deletions, substitutions, or insertions. In this regard, applicant has not enabled the scope of the invention as claimed for those sequences.

The claims are drawn to a method of preparing fusion polypeptides consisting of timothy grass pollen allergens comprising in pertinent part: providing "a" polynucleotide encoding the fusion polypeptide. However the written description is not commensurate in scope to the claims that read on a sequence which consists of or comprises "a polynucleotide encoding the fusion polypeptide". The claims recite "a" polynucleotide as

part of the invention. This reads on a single nucleotide as having the ability to encode the fusion polypeptide. However, there does not appear to be an adequate written description in the specification as-filed that is representative of the single nucleotide having the ability to encode the fusion polypeptide consisting of timothy grass pollen allergens.

The written description in this case only sets forth specific timothy grass pollen allergens; therefore the written description is not commensurate in scope with the claims drawn to fragments thereof. Neither the specification nor the claims teach how to define fragments thereof. Neither the claims nor the specification teach how to obtain such fragments. There is no guidance as to what the fragments are; or what fragments can or cannot be used in the method being claimed. The specification does not include structural examples of the fragments. Thus, the resulting fragment could result in a complexes not taught and enabled by the specification. Claim 42 refers to individual components or fragments thereof, however there is no description of the individual components; similarly there is no description of the fragments. *Vas-Cath Inc. V. Mahurkar*, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (*See Vas-Cath* at page 1116). Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 115).

With the exception of specifically named timothy grass pollen allergens, the skilled artisan cannot envision the detailed structure of the fragments thereof, thus conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. An adequate description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. Furthermore, *In The Reagents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of by only their functional activity does not provide an adequate description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of molecules falling within the scope of the claimed genus.

Regarding the state of the prior art, the closet prior art is Vrtala et al., (1996. J. Allergy Clin. Immun. Vol. 97(3): 781-787) teach some specific grass pollen allergens and the DNA coding for three major timothy grass pollen allergens Phl p1, Phl p 2 and Phl p 5, and the construction of the expression plasmids. Vrtala et al., teach cDNA clones transcribed by polymerase chain reaction, plasmids transfected into host cells; and the expression of recombinant allergens from cultured cells wherein the fusion polypeptide is purified and recovered. Therefore Vrtala et al., show that specific polynucleotide sequences are required for encoding the fusion polypeptide. However, Vrtala et al., show the lack of characterization and guidance concerning a variety of polynucleotides comprising a coding sequence encoding a fusion polypeptide. Vrtala et al., teach that there is no relevant immunologic similarity between Phl p1 and Phl p 2,

thus there is no structural relationship between the individual components; therefore the state of the prior art shows the claimed genus is broad and encompasses wide varying species in structure. The skilled artisan would be forced into undue experimentation to make and use the instantly claimed invention. Therefore, one skilled in the art cannot reasonably conclude that applicant had possession of the claimed invention at the time the instant application was filed. There is no description of polynucleotides comprising a coding sequence encoding a fusion polypeptide.

Therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method for determining sequence identity. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of expression. The nucleic acid itself is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016. In view of these considerations, a person skilled in the art would not have viewed the teachings of the specification sufficient to show that applicants were in possession of the claimed method of preparation. Therefore the full breadth of the claims fail to meet the written description provision of 35 USC 112, first paragraph.

Response to Arguments

4. Applicants urge that "a polynucleotide sequence" erase any ambiguity that the Applicants are referring to a plurality of nucleotides encoding the polypeptide of interest. These phrase results in a claim scope that encompasses nucleic acids that comprises

the full-length the sequence of or any portion of the nucleotide sequence. This claim is encompasses any dinucleotide or larger oligonucleotide. Furthermore, when the term "polynucleotide", is used, the specification must be consulted to determine whether or not it includes an **explicit** definition that imposes some lower limit on the size of what is encompassed by the term. Here the specification has no definition, thus there is no lower limit on the size of the polynucleotide, contrary to applicants assertion.

Applicants urge that the Examiner erase the requirement that Applicants must disclose the primary structure of every single polynucleotide amenable to the claimed methodology. It is noted that there is no requirement that Applicants disclose every single polynucleotide. Rather the examiner is requiring that the requirements for Written Description be meet. The "Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, first paragraph, Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111 ,. Friday January 5, 2001, see especially page 1106 3rd column).

Applicants have failed to describe a representative number of species by actual reduction to practice, provide a disclosure of relevant, identifying characteristics, i.e.,

structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus. Thus, applicants arguments are not viewed as being sufficient to show that applicants were in possession of a method of preparing fusion polypeptides consisting of timothy grass pollen allergens for use as immunotherapeutic agents comprising: (a) providing a polynucleotide sequence encoding the fusion polypeptide.

Applicants assert that Figure 2 and Example 2 detail the construction of recombinant hybrid allergens. Both Figure 2 and Example 2 specifically, polynucleotide sequences encoding Phlp1/Phlp5 and/or Phl p2/ Phl p6. It is noted that In *Gostelli*, the Court determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. As previously discussed, the specification does not provide: a teaching of the entire structure, showing that nucleic acids were isolated at the time the invention was made; does not contain a structural characterization of the complete sequence; does not contain an adequate description of the nucleic acids which must encode the polypeptide. Furthermore, the claim language embraces lots of variants and there is no description of the nucleic acids which encodes such, and the state of the prior art shows that the claimed genus is broad and encompasses wide varying species in structure and lacks a function/ structure correlation. Although the MPEP does not define what constitute a sufficient number of representative, the Courts have indicated what do not constitute a representative number species to adequately describe a broad generic. In *Gostelli*, the Court determined that the disclosure of two chemical

compounds within a subgenus did not describe that subgenus. Therefore applicants' argument is not persuasive. Applicants have also failed to point to support for the individual components or fragments thereof. Furthermore neither Figure 2, nor example 2 disclose testing the fusion polypeptide as candidate immunotherapeutic agents by administering said polypeptide to a test animal and selecting as immunotherapeutic agents those fusion polypeptides that induce IgE-blocking antibodies and induce stronger immune responses compared with the individual components or fragments thereof. Therefore applicants' arguments are not persuasive and the rejection is maintained.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 42-43 and 45-47 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a) Claim 42 recites the limitation "the individual components or fragments thereof" in the claim. There is insufficient antecedent basis for this limitation in the claim. Furthermore, it is unclear what the individual components are, since the individual components have not been recited in the claim. It is also unclear what "fragments thereof" is referring too. For example are fragments of the unknown individual components being referred to, or is "fragments thereof referring to something else.

Therefore the metes and bounds of the claim cannot be ascertained and clarification is required to overcome the rejection.

b) Claim 43 recites the limitation "the timothy grass pollen polypeptide" in the claim. There is insufficient antecedent basis for this limitation in the claim.

c) Claim 45 is unclear. It is unclear how "the respective allergens which comprises the fusion allergen". It is unclear what the respective allergens are. It is unclear how the respective allergens which naturally has only one allergen will comprise a fusion allergen. It is unclear what is being accomplished when two fusion allergens are being compared; i.e., comparing the fusion allergens which induce IgE-blocking antibodies and have reduced allergenic activity to respective allergens which comprise the fusion allergen. The amendment has not overcome the rejection.

Response to Arguments

8. The rejection of claims 42-43 and 45-47 under 35 U.S.C. 112, second paragraph, is maintained.

a) Applicants argue that a fusion polypeptide is inherently a fusion of individual components or fragments thereof; therefore the inherency doctrine obviates this ground for rejection. However, an argument drawn to the doctrine of inherency is misplaced. The doctrine of inherency refers the express, implicit, and inherent disclosures of a prior art reference may be relied upon in the rejection of claims under 35 U.S.C. 102 or 103. "The inherent teaching of a prior art reference, a question of fact, arises both in the context of anticipation and obviousness." *In re Napier*, 55 F.3d 610, 613, 34 USPQ2d

1782, 1784 (Fed. Cir. 1995) (affirmed a 35 U.S.C. 103 rejection based in part on inherent disclosure in one of the references). See also *In re Grasselli*, 713 F.2d 731, 739, 218 USPQ 769, 775 (Fed. Cir. 1983). Here, the issue is that the claims have insufficient antecedent basis for "the individual components or fragments thereof" limitation in the are unclear and inherency does not address the lack of antecedent basis problem, nor does it provide clarity to the claim language.

Applicants should make appropriate amendments so as to have clear support or antecedent basis for the terms appearing in the claims. This is necessary in order to insure certainty in construing the claims in the light of the specification, *Ex parte Kotler*, 1901 C.D. 62, 95 O.G. 2684 (Comm'r Pat. 1901). See 37 CFR 1.75, MPEP §608.01(i) and §1302.01. Note that examiner is simply ensuring that the terms and phrases used in claims find clear support or antecedent basis so that the meaning of the terms in the claims may be ascertainable by reference to the description, see 37 CFR 1.75(d)(1).It is suggested that applicants recite: specific polynucleotide sequences which would encode the fusion polypeptide and the individual components, such that one of skill in the art know would what individual components are comprised within fusion polypeptide. It is also suggested that applicants remove the "the" in front of individual components, thereby addressing the lack of antecedent basis problem.

b) It is also suggested that applicants remove the "the" in front of individual components, thereby addressing the lack of antecedent basis problem.

c) The rejection of claim 45 under 35 U.S.C. 112, second paragraph, is maintained for reasons already of record. Applicants assert that the limitation "the respective allergens" in the claims precisely conveys to one skilled in the art its meaning. However it is unclear what the respective allergens are. It is unclear how the respective allergens comprise fusion allergens. It is unclear what is being compared. Applicants' amendments have not addressed these issues. Thus the rejection is maintained and applicants' arguments are not persuasive.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 45-47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ball et al., (WO 95/34578) in view of Vrtala et al., (1996. J. Allergy Clin. Immun. Vol. 97(3): 781-787).

The claims are drawn to a pharmaceutical composition comprising one or more fusion allergens of timothy grass pollen allergens as immunotherapeutic agents, wherein said agents consists of fusion allergens of timothy grass pollen allergens which have been identified by a method comprising the steps of: (a) providing fusion allergens of naturally occurring timothy grass pollen allergens; (b) challenging an immunological model with said fusion allergens; (c) selecting as candidate immunotherapeutic agents,

those fusion allergens which induce IgE-blocking antibodies and have reduced allergenic activity compared with the respective allergens which comprise the fusion allergen.

Ball et al., teach a timothy grass pollen allergen as a recombinant or synthetic protein or polypeptide comprising Phl p1 to enhance the display of antigencity (page 3, lines 33-35). Ball et al., teach the protein or polypeptide may be fused to an additional polypeptide; both polypeptides are expressed as a fusion protein in prokaryotic or eukaryotic cells (page 4, lines 1-4). The recombinant DNA molecule codes for polypeptides which induce an antibody response (page 3, lines 20-25). Ball et al., teach the timothy grass pollen allergens block the crosslinking of IgE; modulate the immune response; and induce tolerance by immunotherapy with a minimum of anaphylactic side effects (page 1, lines 29-35). Therefore, Ball et al., teach that the Phl p1 timothy grass pollen allergen is part of a fusion polypeptide, however Ball et al., do not teach fusion proteins consisting of two or more timothy grass pollen allergens.

Vrtala et al., teach fusion polypeptides do not significantly affect the allergens IgE-binding capacity (page 782, col.1). Vrtala et al., teach the construction of the expression plasmids for Phl p 1, Phl p 2 and Phl p 5 (page 782, col. 1). cDNA clones were transcribed by polymerase chain reaction to DNA fragments coding for the mature allergens (page 782, col. 1). Phl p 1 and Phl p 2, were then inserted as fragments and the plasmids were transfected into *E.coli* host cells (page 782, col.1). Thus Vrtala et al., teach protein having at least two timothy grass pollen allergens. Phl p1, Phl p2 and Phl p5 are used for sensitization determination (page 781-2, col.2-1). Vrtala et al., teach

grass pollen allergen Phl P1 is a target for IgE antibodies in more than 95% of patients. Vrtala et al., teach Phl p5 is particularly important because of its extremely high IgE-binding capacity; and PhlP2 represents a low molecular weight allergen for 60% of patients (page 781, col.1-2).

Therefore it would have been prima facie obvious at the time of applicants' invention to apply Vrtala et al's recombinant Phl p1, Phl p2 and Phl p5 to Ball et al's pharmaceutical composition or hybrid allergen in order to enhance antigencity. One of ordinary skill in the art would have a reasonable expectation of success by including additional timothy grass pollen allergens fusion polypeptides because the allergens act as the target for IgE antibodies and are important because of their extremely high IgE-binding capacity, and Ball et al., teach the desire to effect antigenicity, and the binding of IgE using fusion polypeptides. Furthermore, no more than routine skill would have been required when Ball et al., teach that timothy grass pollen allergens are amenable to being comprised within fusion proteins and/or hybrid polypeptides and are amenable to fusion with any other expressible polypeptide, while Vrtala et al., teach these same timothy grass pollen allergens are expressible in prokaryotic or eukaryotic cells, thus there is a reasonable expectation of success when no more than routine skill would have been required to create a fusion or hybrid polypeptide comprising one or more timothy grass pollen allergens that do not significantly affect the allergens IgE-binding capacity. Finally it would have been prima facie obvious to combine the invention of Ball et al., and Vrtala et al., to advantageously achieve at fusion polypeptides or hybrid allergens that block the crosslinking of IgE;

modulate the immune response; and induce tolerance by immunotherapy with a minimum of anaphylactic side effects.

Response to Arguments

10. In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, it was prima facie obvious at the time of applicants' invention to apply Vrtala et al's recombinant Phl p1, Phl p2 and Phl p5 to Ball et al's pharmaceutical composition or hybrid allergen in order to enhance antigencity. One of ordinary skill in the art would find motivation because there was a reasonable expectation of success indicated by Ball et al., to incorporate additional expressible polypeptides. There is no teaching that the additional polypeptides can be timothy grass pollen allergens, since they are expressible; act as the target for IgE antibodies; are important because of their extremely high IgE-binding capacity, and effect antigenicity. Therefore, contrary to applicants' assertions, the Ball et al., and Vrtala et al., provide sufficient suggestion, teaching and motivation.

Applicants argue that prior to the current invention, no one has taught nor suggested that the fusion of hybrid allergens can produce immunotherapeutic agents

more desirable than the respective component allergens and that such was indeed a surprise. However, Applicants admit the Ball et al., teach a fusion protein comprising a fusion of one timothy grass allergen. Therefore Ball et al., meet the limitation of the claims. The administration is irrelevant since the claims are drawn to a product, not a method of administration. Furthermore, the use of the fused polypeptides is irrelevant, because the use does not prevent the limitations from being meet.

M.P.E.P 2113 [R-1] entitled Product-by-Process Claims states that such claims are not limited to the manipulations of the recited steps, only the structure implied by the steps. "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) (citations omitted) (Claim was directed to a novolac color developer. The process of making the developer was allowed. The difference between the inventive process and the prior art was the addition of metal oxide and carboxylic acid as separate ingredients instead of adding the more expensive pre-reacted metal carboxylate. The product-by-process claim was rejected because the end product, in both the prior art and the allowed process, ends up containing metal carboxylate. The fact that the metal carboxylate is not directly added, but is instead produced in-situ does not change the end product.). The structure implied by the process steps should be considered when assessing the patentability of product-

by-process claims over the prior art, especially where the product can only be defined by the process steps by which the product is made, or where the manufacturing process steps would be expected to impart distinctive structural characteristics to the final product.

Applicants argue that art does not teach fusion proteins of Phl p1 epitopes and expressible proteins so as to reconfigure the epitopic configuration of the allergen thereby allowing it to be used as an immunotherapeutic agent. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies i.e., fusion proteins of Phl p1 epitopes and expressible proteins so as to reconfigure the epitopic configuration of the allergen thereby allowing it to be used as an immunotherapeutic agents are not recited in the rejected claims. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Therefore, applicants' arguments are not persuasive.

"[T]he discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." *Atlas Powder Co. v. Ireco Inc.*, 190 F.3d 1342,1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). Thus the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. *In re Best*, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977). In *In re Crish*, 393 F.3d 1253, 1258, 73 USPQ2d 1364,

1368 (Fed. Cir. 2004), the court held that the claimed promoter sequence obtained by sequencing a prior art plasmid that was not previously sequenced was anticipated by the prior art plasmid which necessarily possessed the same DNA sequence as the claimed oligonucleotides. The court stated that "just as the discovery of properties of a known material does not make it novel, the identification and characterization of a prior art material also does not make it novel." Id. See also MPEP § 2112.01 with regard to inherency and product-by-process claims and MPEP §2141.02 with regard to inherency and rejections under 35 U.S.C. 103. Furthermore, the inherent feature need not be recognized at the time of the prior art.

Applicants' argue that the art does not recognize the use of the epitopes as immunotherapeutic agents. In response to applicant's argument that the art does not appreciate the immunotherapeutic abilities of the allergens, a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. Here the art clearly teach the creation of a fusion allergen wherein said allergen is a fusion protein of one or more timothy grass pollen allergens, since Ball et al., already teach the need to have a fusion polypeptide. Ball et al., teach that timothy grass allergenic proteins such as Phl p1 are amenable to being comprised within fusion proteins and/or polypeptides and can be fused to any other polypeptide that can be expressed as a fusion protein in prokaryotic or eukaryotic cells. Furthermore, Vrtala et al., teach polypeptides that can be expressed in prokaryotic or eukaryotic cells, thus no

more than routine skill would have been required to create a hybrid polypeptide comprising at least two timothy grass allergens. Therefore applicants' arguments are not persuasive and the rejection is maintained.

Claims 42-43 are drawn to a method of preparing fusion polypeptides consisting of timothy grass pollen allergens for use as immunotherapeutic agents comprising: (a) providing a polynucleotide sequence encoding the fusion polypeptide; (b) introducing said polynucleotide sequence into a host cell; (c) culturing the host cell obtained in b) under conditions such that the fusion polypeptide is expressed; (d) recovering the expressed fusion polypeptide from the cultured host cell; and (e) testing the fusion polypeptide as candidate immunotherapeutic agents by administering said polypeptide to a test animal and selecting as immunotherapeutic agents those fusion polypeptides that induce IgE-blocking antibodies and induce stronger immune responses compared with the individual components or fragments thereof.

Conclusion

11. No claims allowed.

12. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is 571-272-0859. The examiner can normally be reached on Monday-Thursday and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Jeffery Siew, can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Ja-Na Hines
May 30, 2007